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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,080	04/27/2001	Wendy Naimark	00-0238	1601

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EXAMINER	
NGUYEN, DAVE TRONG	
ART UNIT	**PAPER NUMBER**
1632	13

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.	Applicant(s)
09/845,080	Naimark
Examiner	**Art Unit**
Dave Nguyen	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED *Jun 11, 2003* FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see NOTE below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☒ Applicant's reply has overcome the following rejection(s):
rejections under 112, first paragraphs, the 102(e) rejection and/or 103 rejection using the Pachuk reference.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
of the remaining rejections. See the attached paper for more details.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *NONE*

Claim(s) objected to: _____

Claim(s) rejected: *1-3, 7, 8, 10-15, 17, and 37-42*

Claim(s) withdrawn from consideration: *4, 5, and 9*

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ .

10. ☐ Other:

Claim 1 has been amended by the amendment filed June 11, 2003

Claims 1, 2, 7, 9-15, 17, 37-42 readable on:

A method of using suitable polymer microparticles to protect a pharmaceutical effectiveness of a pharmaceutically active agent, comprising:

Providing a pharmaceutically acceptable suspension comprising a pharmaceutically active agent, *e.g.,* drugs, protein, DNA, plasmids, or any biologically active agents known in the prior art, commingled (hereby interpreted as the act of bringing together the DNA and polymeric micropartiles within a suspension, whereby the DNA are being dispersed within the polymeric microparticles, with suitable polymer microparticles, *e.g.,* polystyrene based polymer, and a metal compound, *e.g.,* any metal compound including those metal compounds that form basic components of a metallic medical delivery device,

wherein said polymer microparticles result in a pharmaceutical effectiveness of the pharmaceutically active agent in the absence of the microparticles,

Are rejected under 35 USC 102(e) as being anticipated by Mathiowitz (US 6,248,720).

Mathiowitz teaches the identical method on Table 1, column 11, column 13, lines 21-45, column 14, lines 33-49, column 23, and Example 2. Size and concentration of polymeric microparticles are disclosed on columns 7 and 8. Blends of polystyrene based microparticles are disclosed on column 11, line 50.

Absent evidence to the contrary and give all of the limitations are met by the disclosure of the recited reference, the disclosed microparticles as employed in the delivery method of Mathiowitz would enhance the pharmaceutical effectiveness of the delivered agent such as drugs and/or DNA in the absence of the microparticles.

Applicant's response in the first amendment after final (pages 8-9) has been considered by the examiner but is not found persuasive for the same reasons as set forth in the final rejection. Applicant mainly asserts that the limitation of a suspension which comprises the DNA (pharmaceutically active agent) and the polymeric miroparticles being "commingled" is not the same as the limitation of a suspension of the DNA being encapsulated within polymeric micoparticles. Applicant further points out a working example (Example 1) as the evidence for the distinction. In response, the examiner maintains that not only the working example and/or the cited paragraph, at the time the invention was made, does not necessarily limit applicant convenient interpretation of the rejected claims in the response as of June 11, 2003, the as-filed specification does not provide any written support in order to define the metes and bounds of the "commingled" as being limited only to any suspension comprising a mixture of DNA and polymeric microparticles, wherein the DNA is not encapsulated within polymeric microparticles. In fact, the as-filed specification states on page 12 bridging page 13:

> To form the suspension of the present invention, the microparticles and the pharmaceutically active agent are commingled in a liquid medium by essentially any known mean, including stirring, shaking, and so forth.

As such and to the extent that the suspension of Mathiowitz does contain DNA plasmids being brought together or mixed within the matrix of polymeric microparticles contained in a suspension, which "bringing together" or "mixing together" is reasonably interpreted as being embraced by the commingled activities between the DNA and polymeric micriparticles as recited in the claims, the Mathiowitz remain properly used in the remaining 102(e) rejection.

Claims 1-3, 7-8, 10-15, 17, 37-42 readable on

A method of using suitable polymer microparticles to protect a pharmaceutical effectiveness of a pharmaceutically active agent, comprising:

Providing a pharmaceutically acceptable suspension comprising a pharmaceutically active agent, *e.g.,* drugs, protein, DNA, plasmids, or any biologically active agents known in the prior art, commingled with suitable polymer microparticles, *e.g.,* polystyrene based polymer,

and contacting said pharmaceutically acceptable suspension to a stainless steel based metal which is a component of a medical delivery device, wherein said polymer microparticles result in a pharmaceutical effectiveness of the pharmaceutically active agent in the absence of the microparticles,

remain rejected under 35 USC 103(a) as being unpatentable over Mathiowitz taken with Barry (WO 01/30403).

The rejection of the base claims is applied here as indicated above. To the extent that Mathiowitz does not teach that a metallic or polymer coated medical delivery device is employed to deliver the biologically active agent encapsulated controlled release polymeric microparticles, Both Barry and Pinchuk (entire disclosure) teach that it is well-established in the prior art that medical delivery devices including those of metallic based catheter and/or polymer coated metallic based catheters are routinely employed for delivery of biologically active agent to any desired cell *in vivo.*

It would have been obvious for one of ordinary skill in the art to employ any medical delivery device available in the prior art including those described in the cited references to deliver the encapsulated active agents of Mathiowitz to a target cell *in vivo.* One of ordinary skill in the art of controlled released carriers and medical techniques would have been motivated to employ the medical devices of Barry and Pinchuk because both Barry and Pinchuk teach that it is well-established in the prior art that medical delivery devices including those of metallic based catheter and/or polymer coated metallic based catheters are routinely employed for delivery of biologically active agent to any desired cell *in vivo,* and teach the advantages of employed their medical delivery devices as a medical tool to deliver any biologically active agent to a cell.

Thus, the claimed invention, as a whole, was *prima facie,* obvious.

Applicant's response in the first amendment after final (pages 8-10) has been considered by the examiner but is not found persuasive for the same reasons as set forth in the final rejection, and the reasons set forth *suppra.* Applicant mainly asserts that the limitation of a suspension which comprises the DNA (pharmaceutically active agent) and the polymeric miroparticles being "commingled" is not the same as the limitation of a suspension of the DNA being encapsulated within polymeric micoparticles. Applicant further points out a working example (Example 1) as the evidence for the distinction. In response, the examiner maintains that the as-filed specification does not provide any written support in order to define the metes and bounds of the "commingled" as being limited only to any suspension comprising a mixture of DNA and polymeric microparticles, wherein the DNA is not encapsulated within polymeric microparticles. As such and to the extent that the suspension of Mathiowitz does contain DNA plasmids being brought together or mixed within the matrix of polymeric microparticles contained in a suspension, which "bringing together" or "mixing together" is reasonably interpreted as being embraced by the commingled activities between the DNA and polymeric micriparticles as recited in the claims, the Mathiowitz remain properly used as the primary reference in the remaining 103 rejection. Furthermore, a skilled artisan at the time the invention was made has to consider all of the relevant prior art at the time the invention was made, and thus, the totality of the prior art has to considered as a whole by one of ordinary skill in the art of using medical devices as carriers of pharmaceutically active agents. Within this context, the Barry reference clearly teaches through out the reference the disadvantages of using medical delivery device that has incompatible polymers or metallic substances being contact with pharmaceutically active agents (page 3 bridging page 4, , page 6, third full par., page 10, first full par., Example 9, page 24, claim 20. As such and given that the Barry reference clearly provides, teaches, and suggests the solution to overcome the disadvantages wherein the solution is employ a layer of more compatible synthetic polymer material to prevent and/or reduce the contact between the pharmaceutical agent and the incompatible components present on the surface of the medical delivery devices, one of ordinary skill I nteh art would have been motivate to employ the pharmaceutical

acceptable suspension of Mathiowitz, which comprises a pharmaceutical active agent being brought together or mixed together within the matrix of pharmaceutically acceptable polymeric microparticles in the delivery method of Barry. One of ordinary skill in the art would have been motivated to do so because the coated layer of the pharmaceutically acceptable polymeric microparticles would necessarily prevent and/or reduce the exposure between the pharmaceutically active agent encapsulated there in and the incompatible component present on the surface of the medical deliver device. Note also that Mathiowitz on column 13 teaches that the DNA/polymer suspension can be brought in contact with a medically delivery device comprising a metallic layer.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **(703) 305-2024**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Deborah Reynolds*, may be reached at **(703) 305-4051.**

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is **(703) 305-7401**.

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Trong Nguyen
Primary Examiner
Art Unit: 1632

DAVE T. NGUYEN
PRIMARY EXAMINER